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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/855,542	05/16/2001	Rajesh Manchanda	BERLX-100	9728

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EXAMINER	
WELLS, LAUREN Q	
ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 03/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/855,542	Applicant(s) MANCHANDA, RAJESH	
	Examiner Lauren Q Wells	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 January 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-14,16-25 and 27-35* is/are pending in the application.

4a) Of the above claim(s) *7,17,23-31 and 35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,8-14,16,18-22 and 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-4, 6-14, 16-25, 27-35 are pending. Claims 7, 17, and 23-31 and 35 are withdrawn from consideration, as they are directed to non-elected subject matter. The Amendment filed 1/27/03, Paper No. 6, cancelled claims 5, 15 and 26, amended claims 1, 7, 11, 17, 23, and 28, added claims 32-35, and amended pg. 3-4 of the specification.

Response to Arguments

Applicant's arguments with respect to the rejection of claims 1-4, 5, 8,-9, 11-14, 16-19, 21-22, and 32-34 under 35 USC 102 and 103 have been considered but are moot in view of the new ground(s) of rejection.

The Applicant's amendment filed 1/27/02, Paper No. 6, wherein claims 5 and 15 were cancelled, is sufficient to overcome the 35 USC 112 rejection in the previous Office Action.

go to pg. 3 →

Election/Restrictions

The Amendment filed 1/17/03, Paper No. 6, amended the claims such that they no longer read on the species searched by the Examiner in the Office Action mailed 11/18/02, Paper No. 5. Thus, the Examiner has extended the search to a composition comprising 99m-Tc, alkali metal iodide salt, and depreotide.

In the previous Office Action, the Examiner stated "The Examiner searched a composition comprising Tc-99m, depreotide, and iodide ions, but no art was found to anticipate or render the composition obvious. Thus, claims directed to these species would be allowable". The Examiner hereby withdraws this statement. The new rejection below teaches a composition comprising Tc-99m, depreotide and iodide ions, and it is respectfully pointed out that potassium iodide produced iodide ions in solution.

Applicant's election with traverse of Group I in Paper No. 5 is acknowledged. The traversal is on the ground(s) that "The kit and the composition contain the same ingredients, one as separate components and one after being mixed. The kit is used to prepare the composition. They are clearly related". This is not found persuasive. While the Examiner agrees that the kit and composition are related, the Examiner contends that these inventions are still patentably distinct, as evidenced by their different classification and the different search that would be required. The Examiner respectfully points out that the composition can be enclosed by any apparatus and that the kit can comprise a multitude of different compositions.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-14, 16, 18-22, 33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for lessening the occurrence of the radionuclide degrading, does not reasonably provide enablement for preventing the occurrence of the radionuclide degrading. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are several guidelines when determining if the specification of an application allows the skilled artisan to practice the invention without undue experimentation. The factors to be considered in determining what constitutes undue experimentation were affirmed by the court in *In re Wands* (8 USPQ2d 1400 (CAFC 1986)). These factors are the quantity of experimentation; the amount of direction or guidance presented in the specification; the presence or absence of working examples; the nature of the invention; the state of the prior art; the level of skill of those in the art; predictability or unpredictability of the art; and the breadth of the claims.

The disclosure of the present invention is directed to a composition comprising radionuclide, a targeting agent, and iodide ions or compounds which generate/release iodide ions and methods of stabilizing compositions by adding iodide ions or compound which generates/releases iodide ions, to compositions comprising targeting agents and radionuclides. A skilled practitioner in the art using the teachings of Miller et al. (6,174,513) would be motivated

to use add salts to reduce or eliminate the occurrence of the radionuclide degrading. However, preventing the occurrence of the radionuclide degrading is inconsistent with what is known in the art since (1) reduction of the occurrence of the radionuclide degrading indicates that the occurrence of the radionuclide degrading is decreased, but not prevented; and (2) elimination of the occurrence of the radionuclide degrading indicates that characteristics of the occurrence of the radionuclide degrading may occur. Furthermore, prevention of the occurrence of the radionuclide degrading indicates that the composition *never* experiences any characteristics associated with the occurrence of the radionuclide degrading. Hence, the amount of guidance present in the specification, the absence of data indicating that the characteristics of the occurrence of the radionuclide degrading do not occur when iodide ions or a compound that generates/releases iodide ions are added to a composition comprising radionuclide and targeting agent, and the state of the prior art indicating that the treatment using inorganic salts and surfactants in composition is possible, all indicate that treatment, not prevention of the occurrence of the radionuclide degrading is possible.

The amount of guidance necessary to perform Applicant's invention would result in undue experimentation because the skilled artisan would be forced to randomly test numerous conditions and amounts of iodide ions and compounds that generate/release iodide ions in composition to determine what compounds and iodide levels in the composition prevents the occurrence of the radionuclide degrading. Hence, the amount of guidance present in the specification fails to present the necessary instruction such that one can readily determine the appropriate method of claims 11-14, 16, 18-22 and 33.

Note: The Examiner reviewed Applicant's specification, but noted that the data does not indicate prevention of the occurrence of the radionuclide degrading.

Deleting the term "prevent" in claim 11 will overcome this rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 6, 10-14, 16, 20-22, 33, and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. (6,174,513) in view of Banerjee et al. (2002/0151598).

The instant invention is directed toward a composition comprising a radionuclide, iodide ions or a compound which releases/generates iodide ions, and a targeting agent selected from a peptide, oligonucleotide, antibody, peptidomimetic, or the formula of instant claim 1, and method of stabilizing a composition comprising adding the iodide ions or a compound which releases/generates iodide ions to a composition comprising the radionuclide and targeting agent.

Miller et al. teach stabilization of peptides and proteins for radiopharmaceutical use, wherein surfactants in combination with salts are used to stabilize the peptides or proteins. Technetium-99m and others are taught as suitable radionuclides. The radiolabeled peptide is used with a pharmaceutically acceptable carrier in a method of performing a diagnostic imaging procedure using a scintillation camera. Saline is taught as a pharmaceutically acceptable carrier. The reference lacks compounds that generate/release iodine ions. See Col. 2, lines 11-22; Col. 3, lines 8-Col. 4, line 59; Col. 8, lines 9-42.

Banerjee et al. teach that tonicity adjusting agent can be added to saline solution to provide the desired ionic strength of the pharmaceutical composition. Potassium and sodium iodide are taught as tonicity adjusting agents which display no or only negligible pharmacological activity after in vivo administration. See [0056].

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add the potassium iodide, taught by Banerjee et al., to the saline solution of Miller et al. because of the expectation of achieving a composition wherein the tonicity can be adjusted to provide high, medium, or low ionic strength without effecting the pharmacological activity of the active agent.

While "a method of stabilizing a composition" is not explicitly stated, the Examiner respectfully points out that the above rejection teaches adding a compound which releases iodide ions to a composition comprising a radionuclide and a targeting agent. Thus, since the same steps are taught for affecting the composition, the method of the above rejection must have the property of stabilizing the composition.

Claims 8-9, 18-19, 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. in view of Banerjee et al. as applied to claims 1-4, 6, 10-14, 16, 20-22, 33 and 34 above, and further in view of Blum et al. (Chest).

Miller et al. and Banerjee et al. are applied as discussed above. The reference lacks depreotide.

Blum et al. teach 99mTC depreotide as a somatostatin analog as an optimal imaging agent in scintigraphy for solitary pulmonary nodes. This compound is taught as having a great sensitivity for diagnosing malignant or benign pulmonary tumors. See abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to teach the protein of the combined references as depreotide, as taught by Blum et al., because of the expectation of achieving an imaging agent that is highly sensitive in diagnosing the malignancy of pulmonary tumors and which does not undergo radiolysis (chemical decomposition of the peptide).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lauren Q Wells whose telephone number is (703) 305-1878. The examiner can normally be reached on M-F (7-5:30), with alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (703)305-1877. The fax phone numbers for

the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

lqw
February 26, 2003

SREENI PADMANABHAN
PRIMARY EXAMINER

3/9/03